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REVIEW

Making the clock tick: the transcriptional landscape of the plant circadian clock [version 1; referees: 2 approved]

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Abstract

Circadian clocks are molecular timekeepers that synchronise internal physiological processes with the external environment by integrating light and temperature stimuli. As in other eukaryotic organisms, circadian rhythms in plants are largely generated by an array of nuclear transcriptional regulators and associated co-regulators that are arranged into a series of interconnected molecular loops. These transcriptional regulators recruit chromatin-modifying enzymes that adjust the structure of the nucleosome to promote or inhibit DNA accessibility and thus guide transcription rates. In this review, we discuss the recent advances made in understanding the architecture of the *Arabidopsis* oscillator and the chromatin dynamics that regulate the generation of rhythmic patterns of gene expression within the circadian clock.

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Introduction

The daily rotation of the Earth generates predictable diurnal changes in light and temperature. Circadian clocks act as endogenous timekeepers to co-ordinate internal physiological responses to match the predicted environmental condition. The plant circadian clock directly regulates a range of output pathways, which includes hormone signalling, hypocotyl development, metabolism, the floral transition, photosynthesis, and the response to biotic and abiotic stress^{1–3}. Accordingly, plants with an internal clock that matches the external environment (~24 hours) have enhanced photosynthesis and survival compared to plants with a clock that does not match the external environment⁴.

Endogenous circadian rhythms are generated through a series of interconnected transcriptional–translational feedback loops, collectively termed the oscillator. Light and temperature signals differentially converge on the plant oscillator through multiple input pathways to provide timing cues in a process termed entrainment^{5,6}. In plants, light signals at dawn are thought to act as the major entraining signal⁷. This review will discuss the recent advances made in understanding the transcriptional architecture of the plant oscillator and the chromatin dynamics driving rhythmic gene expression.

Overview of the oscillator

At the core of the plant oscillator are the morning-expressed, partially redundant MYB domain transcription factors (TFs) CIRCADIAN CLOCK ASSOCIATED 1 (CCA1) and LATE ELONGATED HYPOCOTYL (LHY)^{8–10}. CCA1/LHY directly antagonise most clock gene expression through binding to the evening element (EE) motif within the promoter^{11–13}. One target of CCA1/LHY-repressive activity is the *PSEUDO-RESPONSE REGULATOR (PRR) TIMING OF CAB EXPRESSION (TOC1)*^{8,9,14}. CCA1/LHY-repressive activity restricts *TOC1* expression to a window around dusk. At dusk, *TOC1* accumulates and reciprocally represses *CCA1/LHY* expression in addition to other clock genes^{15,16}. This mutual antagonism between CCA1/LHY and *TOC1* defines the central loop of the *Arabidopsis* oscillator^{7,9,17}.

Additional interconnected loops subsequently regulate the activity of the core loop^{7,18}. At dawn, the TFs TEOSINTE BRANCHED CYCLOIDEA-PCF20/22 (TCP20/22) recruit the co-activator LIGHT REGULATED WD 1 (LWD1) to activate *CCA1/LHY* expression¹⁹. LWD1 and its homolog LWD2 are also required to activate the expression of *TOC1* and the related *PRR5*, *PRR7*, and *PRR9*²⁰. *PRR5*, *PRR7*, and *PRR9* directly associate with the *CCA1/LHY* promoter and repress *CCA1/LHY* expression^{21,22}. *PRR9*, *PRR7*, and *PRR5* are sequentially expressed, generating a wave of repressive activity. *PRR9* expression starts at dawn, followed by *PRR7* in the late morning and *PRR5* in the afternoon²². This repressive sequence is re-enforced by the CCA1-related MYB TF REVEILLE8 (RVE8) and its associated homologs, RVE6 and RVE4²³. RVE8 binds to the EE within the *PRR5*, *TOC1*, and *EARLY FLOWERING 4 (ELF4)* promoter and activates gene expression by recruiting the co-activators NIGHT LIGHT-INDUCIBLE AND CLOCK REGULATED 1/2 (LNK1/LNK2)^{24–28}. In the evening, the GARP TF LUX ARRHYTHMO (LUX) and the unrelated proteins ELF3 and ELF4 associate to form the evening

complex (EC)^{29,30}. The EC represses the morning-expressed *PRR7* and *PRR9* and evening-expressed *GIGANTEA (GI)* and *LUX*^{29–34}. LUX and ELF3 have also been recently shown to associate with the promoter of *LNK1/2*, highlighting another potential target of the EC³⁵. Together, this interconnected network of activators and repressors drives rhythmic gene expression within the plant oscillator.

Chromatin dynamics of the circadian clock

The structure of nucleosomes has a fundamental role in regulating gene expression. A nucleosome is a complex of DNA wound around the histone octamer (two H2A-H2B dimers and a H3-H4 tetramer)³⁶. Each histone unit can be post-translationally modified through a suite of chromatin-remodelling enzymes to generate what is collectively called the histone code³⁷. These modifications regulate the accessibility of the DNA through opening or compacting the histone octamer or by providing a binding site for other chromatin-modifying enzymes³⁷. Modifications associated with transcriptional activation include the acetylation of H3 lysine residues (H3Ac) or tri-methylation of H3K4 (H3K4me3), while repressive markers include the tri-methylation of H3K9 (H3K9me3) and H3K27 (H3K27me3)^{38–40}.

The promoter regions of *CCA1*, *LHY*, *TOC1*, *GI*, *PRR9*, and *LUX* all display diurnal changes in histone modifications. The levels of H3K9Ac, H3K14Ac, H3K56Ac, and H3K4me3 within the gene promoter peak at the time of maximum gene activation^{41–44}. Conversely, as gene expression declines, there is a reduction in H3Ac and demethylation of H3K4me3 and an increase in H3K36me2, modifications associated with transcriptional repression⁴². It has also recently been shown that there are global diurnal changes in H3K9Ac, H3K27Ac, and H3S28P in the promoters of genes associated with the circadian clock and sugar signalling⁴⁵. Additionally, the association of RVE8 to the *TOC1* promoter is associated with hyperacetylation while the association of CCA1 to the *TOC1* promoter correlates with hypoacetylation^{25,41}. Diurnal post-translational modification of histones thus has a fundamental role in generating the rhythmic patterns of gene expression within the oscillator.

The factors regulating these histone modifications are beginning to be understood. *PRR5*, *PRR7*, and *PRR9* directly recruit the Groucho/Tup1 co-repressor TOPLESS (TPL) through an ethylene amphiphilic repression (EAR) domain to repress *CCA1/LHY* expression⁴⁶. TPL belongs to a multi-gene family of co-repressors that recruit the histone deacetylase (HDA)19 and/or the closely related HDA6 to facilitate gene silencing⁴⁷. Unlike the other PRRs, *TOC1* lacks an EAR domain and cannot directly interact with TPL⁴⁶. The mechanisms mediating *TOC1* repression are therefore unknown. Alongside the PRRs, the EC has also recently been shown to interact with chromatin-remodelling enzymes. ELF3 can co-precipitate with MUT9-like kinase 1–4 (MLK1–4), which promotes the phosphorylation of H3T3^{48,49}. H3T3P is associated with heterochromatin formation and gene silencing⁴⁹. *mlk1–4* single and combination loss-of-function mutants displayed a longer circadian period⁴⁸. In contrast, loss of function in ELF3, ELF4, or LUX all display circadian arrhythmicity^{50–53}. Thus, the EC may recruit other co-repressors to repress gene expression.

Other chromatin-remodelling enzymes have also been associated with the plant oscillator. The histone acetyltransferase (HAT) TAF1 and the HDA HD1 regulates the acetylation and de-acetylation of the *TOC1* and *CCA1* promoter, respectively⁴⁴. However, TAF1 and HDA1 loss-of-function mutants had only a small effect on *TOC1* and *CCA1* expression. *Arabidopsis* has 12 HATs and 18 HDAs, and within each respective class functional redundancy has been observed^{54–56}. HATs and HDAs are therefore likely to be acting redundantly within the clock. Alongside HATs and HDAs, histone methylases and demethylases have also been implicated within the clock. The H3K4me3 methylase SET DOMAIN GROUP 2 (SDG2/ATR3) aides clock gene expression and the ability of TOC1 to associate with DNA⁴². The histone demethylase JUMONJI DOMAIN CONTAINING 5 (JMJD5, also referred to as JM30) displays diurnal regulation with expression peaking in the evening⁵⁷. JMJD5 mutants have a shortening of circadian period, suggesting that JMJD5 has a regulatory role within the oscillator^{57,58}. Remarkably, *Arabidopsis* JMJD5 has retained conserved functional activity with its human orthologue, which functions within the mammalian clock⁵⁷. However, the mammalian JMJD5 lacks canonical demethylase activity⁵⁹. Further work is needed to understand the functional activity of JMJD5 and its role within the *Arabidopsis* clock. It has also been recently shown that 17 different chromatin-remodelling enzymes display diurnal patterns of expression⁶⁰, further intertwining the relationship between the clock and chromatin remodellers. In summary, the concerted activities of a broad range of histone-modifying enzymes are required within the clock to facilitate the transcriptional regulatory activity of the plant oscillator.

Conclusions and perspectives

In recent years, much progress has been made in connecting the individual components of the oscillator into an interconnected transcriptional network. However, many questions still persist over the mechanisms of transcriptional regulation. The association of RVE8 to the *TOC1* promoter correlates with hyperacetylation, but neither RVE8 nor LNK1/2 have domains that could recruit HAT directly^{25,27}. The repressive mechanisms of the core components CCA1/LHY and TOC1 are also poorly understood. TOC1 has been recently shown to co-occupy *PHYTOCHROME INTERACTING FACTOR 3* (*PIF3*) target promoters and inhibit PIF3-mediated gene activation⁶¹. However, whether this is achieved by passively inhibiting HAT recruitment or by actively recruiting co-repressors through an unidentified repression domain is unknown. It also remains unclear whether CCA1/LHY repress gene expression passively or actively, with both mechanisms being proposed in a temporal-dependent manner^{13,41}. Furthermore, CCA1 and LHY are often grouped together and viewed as a joint operator within the clock. However, CCA1 and LHY have been shown to have distinct roles within the clock^{17,62}. Future work could investigate the extent of functional overlap between CCA1/LHY.

One noticeable shortage in the plant clock when compared to the mammalian or fungal circadian clock are transcriptional

activators^{63,64}. CCA1/LHY, TOC1, and the plant-specific protein GI were all proposed to act as transcriptional activators within the oscillator^{14,21,65}. However, these have now been shown to be an indirect relationship or an effect caused by the mutant background used^{12,13,18,66}. In eukaryotes, the default state of gene expression is often one of a repressive nature⁶⁷, so transcriptional activators would be expected within the oscillator.

The discovery of the RVE8/LNKs^{25,27} and the TCP/LWD complex¹⁹ has provided some answers to the mechanisms of transcriptional activation within the oscillator. However, recent mathematical modelling of the oscillator that incorporated RVE8 has shown a non-reliance of the oscillator on transcriptional activation¹⁸. The activation of the oscillator genes could be sourced externally. The transcript induction of *CCA1*, *LHY*, *GI*, *PRR9*, *PRR7*, *LNK1*, *LNK2*, *ELF3*, and *ELF4* are all positively regulated by light^{68–72}. Additionally, the expression of *LUX*, *PRR7*, and *PRR9* is activated in a temperature-dependent manner^{73,74}. Thus, external environmental signals may participate in gene activation within the clock, while the repressive circuitry of the clock acts to antagonise and attenuate these external gene activation pathways. What is notable in this is the finding that a large proportion of transcription factors are rhythmic and a subset of those can modulate clock parameters⁷⁵. Together, it appears that known activators within the clock act to fine-tune prevailing environmental antagonism as a form of signal integration.

Transcriptional regulators and the associated chromatin landscape governing transcriptional regulation are only one level nestled within a multi-layered regulatory network. Post-translational modifications, nucleocytoplasmic partitioning, RNA splicing, and protein degradation all have their own essential role in aiding rhythm generation^{76–78}. It is only through the integration of all of these layers of activity that the plant clock can generate and sustain robust rhythms and facilitate the response to diurnal changes in the environment.

Competing interests

The authors declare that they have no competing interests.

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References



1. **F** Greenham K, McClung CR: Integrating circadian dynamics with physiological processes in plants. *Nat Rev Genet.* 2015; 16(10): 598–610.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
2. Müller LM, von Korff M, Davis SJ: Connections between circadian clocks and carbon metabolism reveal species-specific effects on growth control. *J Exp Bot.* 2014; 65(11): 2915–23.
[PubMed Abstract](#) | [Publisher Full Text](#)
3. Sanchez A, Shin J, Davis SJ: Abiotic stress and the plant circadian clock. *Plant Signal Behav.* 2011; 6(2): 223–31.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
4. **F** Dodd AN, Salathia N, Hall A, et al.: Plant circadian clocks increase photosynthesis, growth, survival, and competitive advantage. *Science.* 2005; 309(5734): 630–3.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
5. Boikoglou E, Ma Z, von Korff M, et al.: Environmental memory from a circadian oscillator: the *Arabidopsis thaliana* clock differentially integrates perception of photic vs. thermal entrainment. *Genetics.* 2011; 189(2): 655–64.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
6. Millar AJ: Input signals to the plant circadian clock. *J Exp Bot.* 2004; 55(395): 277–83.
[PubMed Abstract](#) | [Publisher Full Text](#)
7. Bujdosó N, Davis SJ: Mathematical modeling of an oscillating gene circuit to unravel the circadian clock network of *Arabidopsis thaliana*. *Front Plant Sci.* 2013; 4: 3.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
8. **F** Mizoguchi T, Wheatley K, Hanzawa Y, et al.: *LHY* and *CCA1* are partially redundant genes required to maintain circadian rhythms in *Arabidopsis*. *Dev Cell.* 2002; 2(5): 629–41.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
9. **F** Alabadi D, Yanovsky MJ, Más P, et al.: Critical role for *CCA1* and *LHY* in maintaining circadian rhythmicity in *Arabidopsis*. *Curr Biol.* 2002; 12(9): 757–61.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
10. Lu SX, Knowles SM, Andronis C, et al.: CIRCADIAN CLOCK ASSOCIATED1 and LATE ELONGATED HYPOCOTYL function synergistically in the circadian clock of *Arabidopsis*. *Plant Physiol.* 2009; 150(2): 834–43.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
11. Harmer SL, Hogenesch JB, Straume M, et al.: Orchestrated transcription of key pathways in *Arabidopsis* by the circadian clock. *Science.* 2000; 290(5499): 2110–3.
[PubMed Abstract](#) | [Publisher Full Text](#)
12. **F** Adams S, Manfield I, Stockley P, et al.: Revised Morning Loops of the *Arabidopsis* Circadian Clock Based on Analyses of Direct Regulatory Interactions. *PLoS One.* 2015; 10(12): e0143943.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
13. **F** Nagel DH, Doherty CJ, Pruneda-Paz JL, et al.: Genome-wide identification of *CCA1* targets uncovers an expanded clock network in *Arabidopsis*. *Proc Natl Acad Sci U S A.* 2015; 112(34): E4802–10.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
14. **F** Alabadi D, Oyama T, Yanovsky MJ, et al.: Reciprocal regulation between *TOC1* and *LHY/CCA1* within the *Arabidopsis* circadian clock. *Science.* 2001; 293(5531): 880–3.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
15. **F** Gendron JM, Pruneda-Paz JL, Doherty CJ, et al.: *Arabidopsis* circadian clock protein, *TOC1*, is a DNA-binding transcription factor. *Proc Natl Acad Sci U S A.* 2012; 109(8): 3167–72.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
16. **F** Huang W, Pérez-García P, Pokhilko A, et al.: Mapping the core of the *Arabidopsis* circadian clock defines the network structure of the oscillator. *Science.* 2012; 336(6077): 75–9.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
17. Ding Z, Doyle MR, Amasino RM, et al.: A complex genetic interaction between *Arabidopsis thaliana* *TOC1* and *CCA1/LHY* in driving the circadian clock and in output regulation. *Genetics.* 2007; 176(3): 1501–10.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
18. Fogelmark K, Troein C: Rethinking transcriptional activation in the *Arabidopsis* circadian clock. *PLoS Comput Biol.* 2014; 10(7): e1003705.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
19. **F** Wu JF, Tsai HL, Joanito I, et al.: LWD-TCP complex activates the morning gene *CCA1* in *Arabidopsis*. *Nat Commun.* 2016; 7: 13181.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
20. **F** Wang Y, Wu JF, Nakamichi N, et al.: LIGHT-REGULATED WD1 and PSEUDO-RESPONSE REGULATOR9 form a positive feedback regulatory loop in the *Arabidopsis* circadian clock. *Plant Cell.* 2011; 23(2): 486–98.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
21. **F** Farré EM, Harmer SL, Harmon FG, et al.: Overlapping and distinct roles of *PRR7* and *PRR9* in the *Arabidopsis* circadian clock. *Curr Biol.* 2005; 15(1): 47–54.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
22. **F** Nakamichi N, Kiba T, Henriques R, et al.: PSEUDO-RESPONSE REGULATORS 9, 7, and 5 are transcriptional repressors in the *Arabidopsis* circadian clock. *Plant Cell.* 2010; 22(3): 594–605.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
23. **F** Hsu PY, Devisetty UK, Harmer SL: Accurate timekeeping is controlled by a cycling activator in *Arabidopsis*. *eLife.* 2013; 2: e00473.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
24. **F** Rawat R, Takahashi N, Hsu PY, et al.: REVEILLE8 and PSEUDO-RESPONSE REGULATORS form a negative feedback loop within the *Arabidopsis* circadian clock. *PLoS Genet.* 2011; 7(3): e1001350.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
25. **F** Farinas B, Mas P: Functional implication of the MYB transcription factor *RYE8/LCL5* in the circadian control of histone acetylation. *Plant J.* 2011; 66(2): 318–29.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
26. **F** Rugnone ML, Faigón Soverna A, Sanchez SE, et al.: *LNK* genes integrate light and clock signaling networks at the core of the *Arabidopsis* oscillator. *Proc Natl Acad Sci U S A.* 2013; 110(29): 12120–5.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
27. Xie Q, Wang P, Liu X, et al.: *LNK1* and *LNK2* are transcriptional coactivators in the *Arabidopsis* circadian oscillator. *Plant Cell.* 2014; 26(7): 2843–57.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
28. **F** Xing H, Wang P, Cui X, et al.: *LNK1* and *LNK2* recruitment to the evening element require morning expressed circadian related MYB-like transcription factors. *Plant Signal Behav.* 2015; 10(3): e1010888.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
29. **F** Nusinow DA, Helfer A, Hamilton EE, et al.: The ELF4-ELF3-LUX complex links the circadian clock to diurnal control of hypocotyl growth. *Nature.* 2011; 475(7356): 398–402.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
30. **F** Herrero E, Kolmos E, Bujdosó N, et al.: EARLY FLOWERING₃ recruitment of EARLY FLOWERING₃ in the nucleus sustains the *Arabidopsis* circadian clock. *Plant Cell.* 2012; 24(2): 428–43.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
31. **F** Kolmos E, Nowak M, Werner M, et al.: Integrating *ELF4* into the circadian system through combined structural and functional studies. *HFSP J.* 2009; 3(5): 350–66.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
32. Kolmos E, Herrero E, Bujdosó N, et al.: A reduced-function allele reveals that *EARLY FLOWERING3* repressive action on the circadian clock is modulated by phytochrome signals in *Arabidopsis*. *Plant Cell.* 2011; 23(9): 3230–46.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
33. **F** Dixon LE, Knox K, Kozma-Bognar L, et al.: Temporal repression of core circadian genes is mediated through *EARLY FLOWERING 3* in *Arabidopsis*. *Curr Biol.* 2011; 21(2): 120–5.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
34. Anwer MU, Boikoglou E, Herrero E, et al.: Natural variation reveals that intracellular distribution of *ELF3* protein is associated with function in the circadian clock. *eLife.* 2014; 3.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
35. Mizuno T, Takeuchi A, Nomoto Y, et al.: The *LNK1* night light-inducible and clock-regulated gene is induced also in response to warm-night through the circadian clock nighttime repressor in *Arabidopsis thaliana*. *Plant Signal Behav.* 2014; 9(3): e28505.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
36. **F** Luger K, Mäder AW, Richmond RK, et al.: Crystal structure of the nucleosome core particle at 2.8 Å resolution. *Nature.* 1997; 389(6648): 251–60.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
37. **F** Venkatesh S, Workman JL: Histone exchange, chromatin structure and the regulation of transcription. *Nat Rev Mol Cell Biol.* 2015; 16(3): 178–89.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
38. Charron JB, He H, Elling AA, et al.: Dynamic landscapes of four histone modifications during deetiolation in *Arabidopsis*. *Plant Cell.* 2009; 21(12): 3732–48.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
39. **F** Zhang X, Clarenz O, Cokus S, et al.: Whole-genome analysis of histone H3 lysine 27 trimethylation in *Arabidopsis*. *PLoS Biol.* 2007; 5(5): e129.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
40. **F** Jiang D, Berger F: Histone variants in plant transcriptional regulation. *Biochim Biophys Acta.* 2017; 1860(1): 123–30.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
41. **F** Perales M, Más P: A functional link between rhythmic changes in

- chromatin structure and the *Arabidopsis* biological clock. *Plant Cell*. 2007; 19(7): 2111–23.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
42. **F** Malapeira J, Khaitova LC, Mas P: **Ordered changes in histone modifications at the core of the *Arabidopsis* circadian clock.** *Proc Natl Acad Sci U S A*. 2012; 109(52): 21540–5.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 43. Song H, Noh YS: **Rhythmic oscillation of histone acetylation and methylation at the *Arabidopsis* central clock loci.** *Mol Cells*. 2012; 34(3): 279–87.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 44. Hemmes H, Henriques R, Jang IC, *et al.*: **Circadian clock regulates dynamic chromatin modifications associated with *Arabidopsis* CCA1/LHY and TOC1 transcriptional rhythms.** *Plant Cell Physiol*. 2012; 53(12): 2016–29.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 45. **F** Baerenfaller K, Shu H, Hirsch-Hoffmann M, *et al.*: **Diurnal changes in the histone H3 signature H3K9ac/H3K27ac/H3S28p are associated with diurnal gene expression in *Arabidopsis*.** *Plant Cell Environ*. 2016; 39(11): 2557–69.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 46. **F** Wang L, Kim J, Somers DE: **Transcriptional corepressor TOPLESS complexes with pseudorepressor regulator proteins and histone deacetylases to regulate circadian transcription.** *Proc Natl Acad Sci U S A*. 2013; 110(2): 761–6.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 47. Zhu Z, Xu F, Zhang Y, *et al.*: ***Arabidopsis* resistance protein SNC1 activates immune responses through association with a transcriptional corepressor.** *Proc Natl Acad Sci U S A*. 2010; 107(31): 13960–5.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 48. **F** Huang H, Alvarez S, Bindbeutel R, *et al.*: **Identification of Evening Complex Associated Proteins in *Arabidopsis* by Affinity Purification and Mass Spectrometry.** *Mol Cell Proteomics*. 2016; 15(1): 201–17.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 49. **F** Wang Z, Casas-Mollano JA, Xu J, *et al.*: **Osmotic stress induces phosphorylation of histone H3 at threonine 3 in pericentromeric regions of *Arabidopsis thaliana*.** *Proc Natl Acad Sci U S A*. 2015; 112(27): 8487–92.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 50. Reed JW, Nagpal P, Bastow RM, *et al.*: **Independent action of ELF3 and phyB to control hypocotyl elongation and flowering time.** *Plant Physiol*. 2000; 122(4): 1149–60.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 51. Hicks KA, Albertson TM, Wagner DR: **EARLY FLOWERING3 encodes a novel protein that regulates circadian clock function and flowering in *Arabidopsis*.** *Plant Cell*. 2001; 13(6): 1281–92.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 52. **F** Doyle MR, Davis SJ, Bastow RM, *et al.*: **The *ELF4* gene controls circadian rhythms and flowering time in *Arabidopsis thaliana*.** *Nature*. 2002; 419(6902): 74–7.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 53. **F** Hazen SP, Schultz TF, Pruneda-Paz JL, *et al.*: **LUX ARRHYTHMO encodes a Myb domain protein essential for circadian rhythms.** *Proc Natl Acad Sci U S A*. 2005; 102(29): 10387–92.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 54. Zhou C, Labbe H, Sridha S, *et al.*: **Expression and function of HD2-type histone deacetylases in *Arabidopsis* development.** *Plant J*. 2004; 38(5): 715–24.
[PubMed Abstract](#) | [Publisher Full Text](#)
 55. **F** Benhamed M, Bertrand C, Servet C, *et al.*: ***Arabidopsis* GCN5, HD1, and TAF1/HAF2 interact to regulate histone acetylation required for light-responsive gene expression.** *Plant Cell*. 2006; 18(11): 2893–903.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 56. Tanaka M, Kikuchi A, Kamada H: **The *Arabidopsis* histone deacetylases HDA6 and HDA19 contribute to the repression of embryonic properties after germination.** *Plant Physiol*. 2008; 146(1): 149–61.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 57. Jones MA, Covington MF, DiTacchio L, *et al.*: **Jumonji domain protein JMJ5 functions in both the plant and human circadian systems.** *Proc Natl Acad Sci U S A*. 2010; 107(50): 21623–8.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 58. Jones MA, Harmer S: **JMJ5 Functions in concert with TOC1 in the *Arabidopsis* circadian system.** *Plant Signal Behav*. 2011; 6(3): 445–8.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 59. Del Rizzo PA, Krishnan S, Triebel RC: **Crystal structure and functional analysis of JMJ5 indicate an alternate specificity and function.** *Mol Cell Biol*. 2012; 32(19): 4044–52.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 60. **F** Lee HG, Lee K, Jang K, *et al.*: **Circadian expression profiles of chromatin remodeling factor genes in *Arabidopsis*.** *J Plant Res*. 2015; 128(1): 187–99.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 61. **F** Soy J, Leivar P, González-Schain N, *et al.*: **Molecular convergence of clock and photosensory pathways through PIF3-TOC1 interaction and co-occupancy of target promoters.** *Proc Natl Acad Sci U S A*. 2016; 113(17): 4870–5.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 62. Gould PD, Locke JC, Larue C, *et al.*: **The molecular basis of temperature compensation in the *Arabidopsis* circadian clock.** *Plant Cell*. 2006; 18(5): 1177–87.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 63. Partch CL, Green CB, Takahashi JS: **Molecular architecture of the mammalian circadian clock.** *Trends Cell Biol*. 2014; 24(2): 90–9.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 64. Baker CL, Loros JJ, Dunlap JC: **The circadian clock of *Neurospora crassa*.** *FEMS Microbiol Rev*. 2012; 36(1): 95–110.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 65. **F** Locke JC, Kozma-Bognár L, Gould PD, *et al.*: **Experimental validation of a predicted feedback loop in the multi-oscillator clock of *Arabidopsis thaliana*.** *Mol Syst Biol*. 2006; 2: 59.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 66. **F** Pokhilko A, Fernández AP, Edwards KD, *et al.*: **The clock gene circuit in *Arabidopsis* includes a repressilator with additional feedback loops.** *Mol Syst Biol*. 2012; 8: 574.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 67. Struhl K: **Fundamentally different logic of gene regulation in eukaryotes and prokaryotes.** *Cell*. 1999; 98(1): 1–4.
[PubMed Abstract](#) | [Publisher Full Text](#)
 68. Covington MF, Panda S, Liu XL, *et al.*: **ELF3 modulates resetting of the circadian clock in *Arabidopsis*.** *Plant Cell*. 2001; 13(6): 1305–15.
[PubMed Abstract](#) | [Free Full Text](#)
 69. Jiao Y, Yang H, Ma L, *et al.*: **A genome-wide analysis of blue-light regulation of *Arabidopsis* transcription factor gene expression during seedling development.** *Plant Physiol*. 2003; 133(4): 1480–93.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 70. Tepperman JM, Hudson ME, Khanna R, *et al.*: **Expression profiling of *phyB* mutant demonstrates substantial contribution of other phytochromes to red-light-regulated gene expression during seedling de-etiolation.** *Plant J*. 2004; 38(5): 725–39.
[PubMed Abstract](#) | [Publisher Full Text](#)
 71. Ito S, Nakamichi N, Kiba T, *et al.*: **Rhythmic and light-inducible appearance of clock-associated pseudo-response regulator protein PRR9 through programmed degradation in the dark in *Arabidopsis thaliana*.** *Plant Cell Physiol*. 2007; 48(11): 1644–51.
[PubMed Abstract](#) | [Publisher Full Text](#)
 72. **F** Li G, Siddiqui H, Teng Y, *et al.*: **Coordinated transcriptional regulation underlying the circadian clock in *Arabidopsis*.** *Nat Cell Biol*. 2011; 13(5): 616–22.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 73. **F** Chow BY, Sanchez SE, Breton G, *et al.*: **Transcriptional regulation of *LUX* by CBF1 mediates cold input to the circadian clock in *Arabidopsis*.** *Curr Biol*. 2014; 24(13): 1518–24.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 74. **F** Karayekov E, Sellaro R, Legris M, *et al.*: **Heat shock-induced fluctuations in clock and light signaling enhance phytochrome B-mediated *Arabidopsis* deetiolation.** *Plant Cell*. 2013; 25(8): 2892–906.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#) | [F1000 Recommendation](#)
 75. Hanano S, Stracke R, Jakoby M, *et al.*: **A systematic survey in *Arabidopsis thaliana* of transcription factors that modulate circadian parameters.** *BMC Genomics*. 2008; 9: 182.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 76. Herrero E, Davis SJ: **Time for a nuclear meeting: protein trafficking and chromatin dynamics intersect in the plant circadian system.** *Mol Plant*. 2012; 5(3): 554–65.
[PubMed Abstract](#) | [Publisher Full Text](#)
 77. **F** Nohales MA, Kay SA: **Molecular mechanisms at the core of the plant circadian oscillator.** *Nat Struct Mol Biol*. 2016; 23(12): 1061–9.
[PubMed Abstract](#) | [Publisher Full Text](#) | [F1000 Recommendation](#)
 78. Staiger D, Shin J, Johansson M, *et al.*: **The circadian clock goes genomic.** *Genome Biol*. 2013; 14(6): 208.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)

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